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10/589,621	10/06/2006	Maria Elena Ferrero	2503-1228	3886

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ART UNIT	PAPER NUMBER
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,621	FERRERO, MARIA ELENA	
	Examiner	Art Unit	
	LAWRENCE E. CRANE	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *June 17, 2008 (amendment)*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 August 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

No claims have been cancelled, claims **1, 5-9 and 15** have been amended, the disclosure and the abstract have not been further amended, and new claims **16 and 17** have been added as per the amendment filed June 17, 2008. No additional or supplemental Information Disclosure Statements (IDSs) have been filed as of the date of the Office action. A reference supplied as an attachment and a declaration filed under 37 C.F.R. §1.132 and signed by Mme. Ferrero filed June 17, 2008 have been considered, and said reference has been made of record on the PTO-892 attached hereto.

Claims **1-17** remain in the case.

Note to applicant: when a rejection refers to a claim **X** at line y, the line number "y" is determined from the claim as previously submitted by applicant in the most recent response including ~~lines deleted by line through~~.

Claims **1-17** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant disclosure has only provided two examples wherein the effectiveness of "po-ATP" in the inhibition of cell division of one class of endothelial cell is disclosed. This showing, together with the previous assertions of applicant's theory of the scope of the pharmaceutical activity of po-ATP, is insufficient as a written description to support claims **1-17** wherein a vast array of combinations of o-ATP with other generic classes of pharmaceuticals has been asserted by applicant to be active against a large number of generic disease conditions, including the generic terms "cancer" and several different cancers, wherein angiogenesis is well known in the art to be a necessary condition to support the growth of the neoplastic tissue. Applicant's assertions are not deemed to be believable because of the absence of direct test evidence showing that the o-ATP in combination with other effective pharmaceuticals have activity against any disease condition in either an intact living host or in an appropriately selected cell culture. See *Ex parte Balzarini et al.* 21, USPQ 2d 1892, 1894 (BPAI, 1991), a decision in its first part standing for the proposition that claims directed to medicinal treatments of diseases in highly unpredictable art areas (cancer and tumour treatments remain highly unpredictable particularly in the area of neoplasms of the nervous

system and the pancreas) are properly rejected under 35 U.S.C. §112, first paragraph as lacking adequate enablement, in the absence of sufficient test data in support of the efficacy of the alleged treatment. See the MPEP at §2107.03 for additional guidance concerning this policy.

Applicant's arguments filed June 17, 2008 have been fully considered but they are not persuasive.

Applicant has argued that examiner has not met the burden of the statute, in particular that examiner has not presented " ,,, any evidence to suggest that the claimed invention does not satisfy the description requirement." This statement is correct, but ignores applicant's prior statement that " sufficient evidence or reasoning to the contrary " (emphasis added) is the proper standard, a standard met by the rejection above wherein "reasoning to the contrary" has been provided. Applicant's other submissions (declaration and reference) and arguments have failed to alter examiner's view that the above rejection remains valid. For these reasons the above rejection has been repeated.

Claims **1-17** are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabled for the inhibition of cell division of a single cell type by the administration of "[periodate] oxidized adenosine triphosphate," does not reasonably provide enablement for the treatment of any neoplastic or other disease condition wherein the inhibition of angiogenesis or any other effect caused by administration of -- po-ATP -- . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in *In re Wands* (858 F.2d 731, 737; 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of "undue experimentation" is appropriate are as follows:

A. The breadth of the claims: The instant claims are directed to the treatment of a vast array of generically defined disease conditions wherein VEGF-induced angiogenesis is effectively inhibited by administration of an effective amount of periodate oxidized ATP (po-ATP), and to pharmaceutical compositions wherein po-ATP is present in combination with a vast array of other medicinally active substances.

B. The nature of the invention: The invention is directed to treating diseases wherein angiogenesis is a necessary part of disease progression and therefore, according to the theory of the disclosure, the inhibition of angiogenesis by administration of po-ATP would be effective in treating the disease.

C. The state of the prior art: Following a review of the art of record it is clear that -- po-ATP -- (defined as the dialdehyde produced by periodate oxidation of ATP) is capable of interfering with certain purinergic receptors, but there is no disclosure in said prior art of the administration of po-ATP alone or in combination with other medicinally active substances to treat atherosclerosis, leukemia, or any other neoplastic disease condition except for lymphoma (Ehrlich's tumor cells) wherein angiogenesis is an essential part of disease development and/or disease progression over time.

D. The level of one of ordinary skill: The ordinary practitioner in the instant art area would be expected to have experience in medical practice and an understanding of biological sciences.

E. The level of predictability in the art: Predictability is inversely proportional to the knowledge of the ordinary practitioner concerning the treatment of the entire spectrum of the disease conditions claimed herein to be effectively treated. Neither the instant disclosure nor the prior art except for one newly cited reference (**Cory et al.**) provide any guidance concerning how to practice the instant claimed method of treatment, thereby rendering the instant art area highly unpredictable.

F. The amount of direction provided by the applicant: The instant disclosure provides only two examples wherein the effect of po-ATP is disclosed as being effective in the inhibition of the cell growth of only one a cell line: human umbilical venous endothelial cells (HUVEC). No additional data is presently of record to support the extrapolation of this data to the instant claimed subject matter wherein o-ATP is administered in combination with a vast array of different classes of medicinally active ingredients to treat a vast array of disease conditions including all possible diseases classified as a "cancer" listed in claim **3** and one of the neoplastic diseases (leukemia) listed in claim **4**.

G. The existence of working examples: Only two working examples have been provided in the disclosure as described in the preceding paragraph. Additional data has been supplied by the declaration filed June 17, 2008 by applicant/Mme. Ferrero.

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure is deemed to be excessive because of the absence of sufficient test data and associated guidance. The absence of sufficient test data means that the ordinary practitioner does not have the guidance necessary to practice the vast array of different disease treatments without undue experimentation.

Applicant's arguments filed June 17, 2008 have been fully considered but they are not persuasive.

Examiner notes with appreciation the additional data submitted by applicant in the form of a declaration filed under 37 C.F.R. §1.132. Examiner has read the declaration careful and notes that the findings appear to confirm the very brief specification with its minimal disclosure of specific embodiments, but do not provide sufficient additional data to enable the generic and subgeneric classes of neoplastic diseases claimed to be effectively treated by the administration of "po-ATP." Examiner respectfully suggests that enabled subject matter is limited to the treatment of the exemplified disease conditions only, noting that the term "lymphoma and leukemia" in claim **4** is subgeneric to two classes of neoplasms, classes wherein the etiologies of the various types of "lymphoma" and types of "leukemia" have not been taken into consideration by the very limited scope of test data provided by applicant originally or in the declaration. Examiner finds that the specific embodiments of the instant file history appear to show considerable future potential, but that the experimental exploration needed to achieve adequate enabling support even for the subject matter of claim **4** has yet to be completed. Applicant is respectfully requested to note that a patent application is not the same as a research proposal. As noted in *Brenner v. Manson* (148 USPQ 689 (S. Ct. 1966)) a patent is granted for work already accomplished and " ... is not a hunting license."

Claims **1, 5-9 and 15-16** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim **1** the term "o-ATP" renders the instant claim incomplete because the meaning of the abbreviation has not been provide in the claim. Examiner suggests that the term should be amended to read -- oxidized ATP (o-ATP) --. In view of the chemical formula of "o-ATP" found at page 11, column 1 of the **Granstein et al. '612** reference (PTO-1449 ref. **1**), examiner also notes that the name "oxidized ATP" is misleading because **Granstein's** o-ATP has been both oxidized and reduced, suggesting that the complete chemical structure should also be displayed as part of claim **1** to insure that the intended meaning of the active ingredient in the claimed method of treatment has been accurately represented. Amendment of the disclosure in a similar fashion is also suggested and would not be found to be new matter. Examiner also notes that "o-ATP" is defined as the 2',3'-dialdehyde produced by periodate oxidation of ATP by applicant in the **Ferrero '737** reference (PTO-1449 ref. **5**), an indication that the abbreviation "o-ATP" does not have an agreed upon meaning in the art. See also claims **5, 6, 9 and 15**.

Applicant's arguments filed June 17, 2008 have been fully considered but they are not persuasive.

Examiner notes applicant's complementary commentary on the above rejection. Unfortunately the above rejection has apparently not been taken seriously. Applicant is respectfully requested to define with particularity the active ingredient with terminology that cannot be mistaken, misinterpreted or otherwise confused with other "oxidized ATP compounds," as is the case in newly added claim **16**.

In claim **5** the Markush group appearing at lines 3-6 is entirely generic and therefore incomplete because the generic terms presented as Markush group members have not been further defined as specific substances and therefore the claims are both unsearchable and lacking in well defined metes and bounds. A similar problem occurs in re the Markush group at the end of claim **6**.

Applicant's arguments filed June 17, 2008 have been fully considered but they are not persuasive.

Examiner notes applicant's argument in response (A Markush group is permitted, therefore this Markush group is OK as is), and finds this argument to be beside the point of the rejection repeated above. As applicant correctly notes, the Markush group must be "properly

supported by the disclosure," a circumstance clearly not applicable herein because the laundry lists of generic terms in the noted Markush groups are not defined by listing defining their specific members. Applicant has failed to define the noted claims with particularity.

Claims **5-8** include the term "preparations" but in reality are claims directed to "pharmaceutical composition[s]." The standard format for this type of claim is as follows: -- A pharmaceutical composition comprising {active ingredient(s)} in combination with a pharmaceutically acceptable carrier.-- Claims **5 and 6** are incomplete because they have not specified a -- pharmaceutically acceptable carrier -- and claims **7 and 8** are lacking proper antecedent basis because the -- pharmaceutically acceptable carrier -- necessary to make the particular forms of pharmaceutical compositions specified therein are not provided for, even generically, in the independent claims.

Applicant's arguments filed June 17, 2008 have been fully considered but they are not persuasive.

Examiner notes the amendments made to claims **5-6** but finds same to be incomplete. Applicant appears to be claiming -- pharmaceutical compositions --, a specialized type of composition wherein the presence of a -- pharmaceutically acceptable carrier -- is required. Because the latter item is not present in either of claims **5 or 6**, dependent claims **7 and 8** now lack proper antecedent basis because the carriers listed in the dependent claims have not been provided for in claims **5 and 6**.

In claims **7 and 8** the term "composition" added at line 1, may or may not be the same as the term " preparation" still found at line 2. An amendment to address the confusion is respectfully requested. See also claim **14** wherein the term "preparation" is also found.

Applicant's arguments with respect to claims **7 and 8** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

In claim **16** the term "method for inhibiting ... human endothelial cells" is incomplete and should be amended to read -- method for inhibiting ... human endothelial cells in a host in need thereof --. Examiner respectfully requests applicant to note that the term "human cell" has been the subject of judicial analysis: the term "human cell" was defined by the Board of Patent

Appeals and Interferences (BPAI) in *Ex parte Balzarini*, 21 USPQ 2d, 1892, 1898 (1991) (see p. 1898, column 2, "Rejection IV") and was found to have a scope encompassing any human cell from individual human cells in culture to a living "human host."

Applicant's arguments with respect to claim **1-15** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments including new claim **16**. Examiner also notes that claim **1** already includes the suggested modification, but that claim **9** presently does not.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

"A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent."

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States."

(e) the invention was described in

(1) an application for patent described under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application filed under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a)."

(f) he did not himself invent the subject matter sought to be patented."

Claims **1-3 and 9-17** are rejected under 35 U.S.C. §102(**b**) as being anticipated by **Cory et al.** (PTO-892 ref. **R**).

The **Cory et al.** reference discloses the effective inhibition of a neoplastic disease condition (Ehrlich tumor cells aka "lymphoma") in the abstract and at page 818, column 1, Table 1, last two entries. According to one source ("Ehrlich tumor cells" search on the WEB via Google) are a variety of "lymphoma." Therefore, the instant claimed subject matter is deemed to have been anticipated.

Applicant's arguments filed June 17, 2008 have been fully considered but they are not persuasive.

Examiner notes applicant's conclusion that "CORY et al. cannot anticipate the claimed invention," because the "Ehrlich tumor" disclosed by "CORY et al." is not a "lymphoma." Examiner takes applicant's point in part and has limited the rejected claim list accordingly, but also refers applicant to the remaining generic claims wherein there is no limitation on the kind of neoplasm to be treated, a circumstance wherein the above rejection continues to apply. For these reasons the above rejection has been repeated.

The following is a quotation of 35 U.S.C. §103(**a**) which forms the basis for all obviousness rejections set forth in this Office action:

> "A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made."

Claims **1-3 and 9-17** are rejected under 35 U.S.C. §103(**a**) as being unpatentable over **Cory et al.** (PTO-892 ref. **R**).

The instant claims are directed to the administration of
-- po-ATP -- for the treatment of diseases wherein "VEGF-induced cell division" occurs and has permitted the development of a blood supply and the vessels necessary for same, and also for treatment of the associated neoplasm or other disease.

The **Cory et al.** reference discloses the effective inhibition of a neoplastic disease condition (Ehrlich tumor cells; e.g. a variety of lymphoma) in the abstract and at page 818, column 1, Table 1, last two entries.

Cory et al. does not expressly disclose the treatment of any other neoplastic disease condition.

The disclosure of the effective treatment of a disease specified at least generically by the instant claims, by a compound well known in the prior art, implies that the mechanism of this treatment, while not specifically disclosed in the prior art, was the effect responsible for the

prior art report. Therefore, the instant cited prior art renders obvious from some to all of the claimed treatments of neoplasms and other diseases wherein po-ATP is the active ingredient.

Therefore, the instant claimed methods of treatment of disease conditions wherein VEGF induces tissue blood supply availability, typically in the development of neoplastic tissue growth, would have been obvious to one of ordinary skill in the art having the above cited reference before him at the time the invention was made.

Applicant's arguments filed June 17, 2008 have been fully considered but they are not persuasive.

Examiner notes that applicant has asserted that the Cory et al. reference only discloses the administration of "periodate oxidized inosine triphosphate" to inhibit the tumor cells of an "Ehrlich tumor." Examiner respectfully disagrees and directs applicant's attention to the abstract wherein the administration of po-ATP and po-ITP are specifically disclosed as being effective. Examiner also directs applicant's attention to the references numbered "4" and "6" cited in the Cory et al. reference wherein the medicinal activity of po-ATP and related compounds is specifically referred to in the titles: see citation "6" at page 822, column 1 of the Cory et al. reference wherein the title reads "Inhibition of Nucleic Acid Synthesis in Ehrlich Tumor Cells by Periodate Oxidized Adenosine and Adenylic Acid," and citation "4" wherein periodate oxidized ATP is specifically named as a Ribonucleotide Reductase Inhibitor. Therefore, examiner finds that applicant's analysis of the prior art to be incomplete and that said prior art continues to be applicable to the instant claims. For these reasons the rejection above has been maintained.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. §1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. §1.136(a) will be calculated from the mailing date of the advisory action. In no

event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. S. Anna Jiang, can be reached at **571-272-0627**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status Information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see < http://pair-direct.uspto.gov >. Should you have questions on access to

the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

/L. E. C./

Examiner, Art Unit 1623

LECrane:lec
09/03/2008

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